

## AMENDMENTS

Please amend the claims as follows.

Please cancel claims 10, 12, 14, 17-32, 58-64, 135-137, 140 and 142.

1. (Currently amended) A method of determining a comparative expression profile in an individual, comprising:

(a) creating a multidimensional space of n dimensions, wherein n represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals;

(b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said n molecules in the individual;

(c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;

~~(a)~~ (d) determining a multidimensional coordinate point representative of the expression levels of a sample of n molecules ~~in a population of molecules~~ in a specimen from said an individual;

~~(b)~~ (e) comparing said multidimensional coordinate point determined in step (d) to [[a]] ~~said health-associated reference expression region of said sample of molecules determined in step (c)~~ ; and

~~(e)~~ (f) determining if said multidimensional coordinate point is within or outside said health-associated reference expression region, wherein said multidimensional coordinate point within said health-associated reference expression region indicates a reference expression profile and wherein said multidimensional coordinate point outside said health-associated reference expression region indicates a perturbed expression profile.

Claims 2-5 (Canceled).

6. (Original) The method of claim 1, wherein said reference expression profile indicates a reference health state in said individual.

7. (Original) The method of claim 1, wherein said perturbed expression profile indicates a disease state in said individual.

8. (Original) The method of claim 1, wherein said perturbed expression profile indicates the course of a disease.

9. (Original) The method of claim 1, wherein said specimen is selected from the group consisting of leukocytes, blood, and serum.

Claims 10 (Canceled).

11. (Original) The method of claim 1, wherein said molecules in said specimen comprise nucleic acids.

Claim 12 (Canceled).

13. (Original) The method of claim 1, wherein said molecules in said specimen comprise polypeptides.

Claim 14 (Canceled).

15. (Original) The method of claim 1, wherein said molecules in said specimen comprise small molecules.

16. (Original) The method of claim 1, further comprising the step of reporting whether a reference expression profile or a perturbed expression profile is indicated.

Claims 17-64 (Canceled)

65. (Currently amended) A method of diagnosing a health state, comprising:

(a) creating a multidimensional space of n dimensions, wherein n represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals;

(b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said n molecules in the individual;

(c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;

~~(a)~~ (d) determining the expression levels of a sample of n molecules in a population of molecules in a specimen from an individual;

(e) determining a multidimensional coordinate point representative of the expression levels of the n molecules determined in step (d);

~~(b)~~ (f) comparing said ~~expression levels~~ multidimensional coordinate point determined in step (e) with [[a]] said health-associated reference expression region determined in step (c) of said sample of molecules; and

~~(e)~~ (g) determining if said ~~expression levels of said sample of molecules~~ multidimensional coordinate point is within or outside said health-associated reference expression region, wherein ~~expression levels~~ said multidimensional coordinate point within said health-associated reference expression region indicates a reference health state and wherein ~~expression levels~~ said multidimensional coordinate point outside said health-associated reference expression region indicates a disease state.

Claims 66-69 (Canceled).

70. (Original) The method of claim 65, wherein said reference expression profile indicates a reference health state in said individual.

71. (Original) The method of claim 65, wherein said perturbed expression profile indicates a disease state in said individual.

72. (Original) The method of claim 65, wherein said perturbed expression profile indicates the course of a disease.

73. (Original) The method of claim 65, wherein said specimen is selected from the group consisting of leukocytes, blood, and serum.

74. (Currently amended) The method of claim ~~[[69]]~~ 65, wherein said ~~target is~~ expression levels are determined by contacting said specimen with an array and measuring the expression levels of said n molecules.

75. (Original) The method of claim 65, wherein said molecules in said specimen comprise nucleic acids.

76. (Currently amended) The method of claim ~~[[69]]~~ 74, wherein said ~~target array~~ comprises nucleic acid ligands.

77. (Original) The method of claim 65, wherein said molecules in said specimen comprise polypeptides.

78. (Currently amended) The method of claim ~~[[69]]~~ 65, wherein said ~~target comprises~~ expression levels are determined by contacting said specimen with antibody ligands and measuring the expression levels of said n molecules.

79. (Original) The method of claim 65, wherein said molecules in said specimen comprise small molecules.

80. (Original) The method of claim 65, further comprising the step of reporting whether a reference expression profile or a perturbed expression profile is indicated.

Claims 81-89 (Canceled).

90. (Currently amended) A method of diagnosing a health state in an individual, comprising:

(a) creating a multidimensional space of n dimensions, wherein n represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals;

(b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said n molecules in the individual;

(c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;

~~(a)~~ (d) determining the expression levels of a sample of n molecules in a population of molecules in a specimen from an individual;

(e) determining a multidimensional coordinate point representative of the expression levels of the n molecules determined in step (d);

~~(b)~~ (f) comparing said ~~expression levels~~ multidimensional coordinate point determined in step (e) with [[a]] said health-associated reference expression region determined in step (c) of said sample of molecules; and

~~(e)~~ (g) determining if said ~~expression levels of said sample of molecules~~ multidimensional coordinate point is within or outside said health-associated reference expression region, wherein ~~expression levels~~ said multidimensional coordinate point within said health-associated reference expression region indicates a reference health state and wherein ~~expression levels~~ said multidimensional coordinate point outside said health-associated reference expression region indicates a perturbed health state.

Claims 91-94 (Canceled).

95. (Original) The method of claim 90, wherein said perturbed health state indicates a disease state in said individual.

96. (Original) The method of claim 90, wherein said perturbed expression profile indicates the course of a disease.

97. (Original) The method of claim 90, wherein said specimen is selected from the group consisting of leukocytes, blood, and serum.

98. (Currently amended) The method of claim [[94]] 90, wherein said ~~target is~~ expression levels are determined by contacting said specimen with an array and measuring the expression levels of said n molecules.

99. (Original) The method of claim 90, wherein said molecules in said specimen comprise nucleic acids.

100. (Currently amended) The method of claim [[94]] 98, wherein said ~~target array~~ comprises nucleic acid ligands.

101. (Original) The method of claim 90, wherein said molecules in said specimen comprise polypeptides.

102. (Currently amended) The method of claim [[94]] 90, wherein said ~~target comprises~~ expression levels are determined by contacting said specimen with antibody ligands and measuring the expression levels of said n molecules.

103. (Original) The method of claim 90, wherein said molecules in said specimen comprise small molecules.

104. (Original) The method of claim 90, further comprising the step of reporting whether a reference expression profile or a perturbed expression profile is indicated.

Claims 105-137 (Canceled).

138. (Currently amended) A computer apparatus, comprising:

a processor;

main memory in communication with said processor; and

a comparative expression profiler in communication with said main memory configured to carrying out the computer-executed steps of:

(a) creating a multidimensional space of  $n$  dimensions, wherein  $n$  represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals;

(b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said  $n$  molecules in the individual;

(c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;

~~(a)~~ (d) determining a multidimensional coordinate point representative of the expression levels of a sample of  $n$  molecules from an individual; and

~~(b)~~ (e) comparing said multidimensional coordinate point determined in step (d) with [[a]] said health-associated reference expression region determined in step (c), wherein said multidimensional coordinate point within said health-associated reference expression region indicates a reference expression profile and wherein said multidimensional coordinate point outside said health-associated reference expression region indicates a perturbed expression profile.

139. (Original) The computer apparatus of claim 138, wherein said comparative expression profiler further is configured to carry out the computer-executed step of determining said expression level of said molecule.

Claim 140 (Canceled).

141. (Currently amended) A computer-readable medium having stored thereon a plurality of sequences of instructions, said plurality of sequences of instructions including sequences of instructions which, when executed by a processor, cause said processor to perform the steps of:

(a) creating a multidimensional space of  $n$  dimensions, wherein  $n$  represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals;

(b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said  $n$  molecules in the individual;

(c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;

~~(a)~~ (d) determining a multidimensional coordinate point representative of the expression levels of a sample of  $n$  molecules from an individual; and

~~(b)~~ (e) comparing said multidimensional coordinate point determined in step (d) with [[a]] said health-associated reference expression region determined in step (c), wherein said multidimensional coordinate point within said health-associated reference expression region indicates a reference expression profile and wherein said multidimensional coordinate point outside said health-associated reference expression region indicates a perturbed expression profile.

Claim 142 (Canceled).

143. (Withdrawn) A carrier wave carrying instructions for a processor, said instructions which, when executed by said processor, cause said processor to perform the steps of:

(a) determining a multidimensional coordinate point representative of the expression levels of a sample of molecules from an individual; and

(b) comparing said multidimensional coordinate point with a health-associated reference expression region, wherein said multidimensional coordinate point within said health-associated reference expression region indicates a reference expression profile and wherein said multidimensional coordinate point outside said health-associated reference expression region indicates a perturbed expression profile.



144. (Currently amended) A method of diagnosing a health state in an individual, comprising:

(a) creating a multidimensional space of n dimensions, wherein n represents the number of molecules being analyzed in a specimen from each individual in a population of reference individuals;

(b) determining a multidimensional coordinate point for each individual in said population of reference individuals, wherein said multidimensional coordinate point is representative of the expression levels of said n molecules in the individual;

(c) determining in said multidimensional space a health-associated reference expression region for said multidimensional coordinate points determined for said population of reference individuals;

~~(a)~~ (d) contacting a leukocyte specimen from an individual with a target;

~~(b)~~ (e) determining the expression levels of a sample of n molecules in a population of molecules in said leukocyte specimen;

(f) determining a multidimensional coordinate point representative of the expression levels of the n molecules determined in step (e);

~~(e)~~ (g) comparing said expression levels multidimensional coordinate point determined in step (f) with [[a]] said health-associated reference expression region determined in step (c);  
and

~~(d)~~ (h) determining if said expression levels of said sample of molecules multidimensional coordinate point is within or outside said health-associated reference expression region, wherein expression levels within said health-associated reference expression region indicates a reference health state and wherein expression levels outside said health-associated reference expression region indicates a perturbed health state.

145. (Previously presented ) The method of claim 144, wherein said perturbed health state indicates a disease state in said individual.

146. (Previously presented) The method of claim 144, wherein said perturbed expression profile indicates the course of a disease.

147. (Previously presented) The method of claim 144, wherein said target is an array.

148. (Previously presented) The method of claim 144, wherein said molecules in said specimen comprise nucleic acids.

149. (Previously presented) The method of claim 144, wherein said target comprises nucleic acid ligands.

150. (Previously presented) The method of claim 144, wherein said molecules in said specimen comprise polypeptides.

151. (Previously presented) The method of claim 144, wherein said target comprises antibody ligands.

152. (Previously presented) The method of claim 144, wherein said molecules in said specimen comprise small molecules.

153. (Previously presented ) The method of claim 144, further comprising the step of reporting whether a reference expression profile or a perturbed expression profile is indicated.

Please add the following new claims.

154. (New) The method of claim 1, wherein n is 3 or more molecules.

155. (New) The method of claim 1, wherein n is 5 or more molecules.

156. (New) The method of claim 1, wherein n is 10 or more molecules.

157. (New) The method of claim 1, wherein n is 20 or more molecules.

158. (New) The method of claim 1, wherein n is 50 or more molecules.

159. (New) The method of claim 1, wherein n is 100 or more molecules.

160. (New) The method of claim 1, wherein n is 200 or more molecules.
161. (New) The method of claim 1, wherein n is 500 or more molecules.
162. (New) The method of claim 1, wherein n is 1000 or more molecules.
163. (New) The method of claim 65, wherein n is 3 or more molecules.
164. (New) The method of claim 65, wherein n is 5 or more molecules.
165. (New) The method of claim 65, wherein n is 10 or more molecules.
166. (New) The method of claim 65, wherein n is 20 or more molecules.
167. (New) The method of claim 65, wherein n is 50 or more molecules.
168. (New) The method of claim 65, wherein n is 100 or more molecules.
169. (New) The method of claim 65, wherein n is 200 or more molecules.
170. (New) The method of claim 65, wherein n is 500 or more molecules.
171. (New) The method of claim 65, wherein n is 1000 or more molecules.
172. (New) The method of claim 90, wherein n is 3 or more molecules.
173. (New) The method of claim 90, wherein n is 5 or more molecules.
174. (New) The method of claim 90, wherein n is 10 or more molecules.
175. (New) The method of claim 90, wherein n is 20 or more molecules.
176. (New) The method of claim 90, wherein n is 50 or more molecules.
177. (New) The method of claim 90, wherein n is 100 or more molecules.
178. (New) The method of claim 90, wherein n is 200 or more molecules.
179. (New) The method of claim 90, wherein n is 500 or more molecules.

180. (New) The method of claim 90, wherein n is 1000 or more molecules.
181. (New) The method of claim 144, wherein n is 3 or more molecules.
182. (New) The method of claim 144, wherein n is 5 or more molecules.
183. (New) The method of claim 144, wherein n is 10 or more molecules.
184. (New) The method of claim 144, wherein n is 20 or more molecules.
185. (New) The method of claim 144, wherein n is 50 or more molecules.
186. (New) The method of claim 144, wherein n is 100 or more molecules.
187. (New) The method of claim 144, wherein n is 200 or more molecules.
188. (New) The method of claim 144, wherein n is 500 or more molecules.
189. (New) The method of claim 144, wherein n is 1000 or more molecules.